Q 1 - 1

Palisading granuloma

Foci of collagen degeneration surrounded with histiocytes arranged in a palisading pattern

1. Granuloma annulare
2. Necrobiosis lipoidica
3. Rheumatoid nodule
4. Actinic granuloma
5. Necrobiotic xanthogranuloma
6. Gout

Q 1 - 2

Subject: Day: Date: / /

① Pripulonecrotic tubercul:d

② Sycotic granuloma

③ Cat scratch disease

④ Allerg:c and wegner's granulomatosis

Q 2 -1

Necrobiotic disorders

A group of cutaneous granulomas with a comon histological picture

Histocytes arranged in a palisading pattern surrounding central zone of collagen degeneration

* Mucinous in G.A
* Necrobiotic in NRL
* Fibrinoid in RN

Q2-2

① Granuloma annulare (G.A)

is self limited, chronic necrobiotic dermal papules arranged in an annular configuration

*Clinically

① localized G.A

*Variants ① Generalized G.A

② Subcutaneous nodular G.A

③ perforating G.A

④ Erythematous G.A

Q 2-3

Subject Day Date / /

(5) Dep Destructive C-Q

(6) C. multiform

Histopathology: Mucin can be seen with collagen degeneration as faint feathery blue in routine stain

* pathogenesis

(1) vasculitis in the dermal blood v.

(2) trauma. post BCG vaccine

(3) Delayed type hypersensitivity

Q 2 - 4

x Associations

x DM & generalized GA

x Mauriac's syndrome

x Association with MSL, sarcoid and ATDs

x treatment:

① steroid

② Destructive (a) cryotherapy

(b) surgical (c) laser destruction

(d) Radiotherapy.

③ systemic. methotrexate. dapson

Q 2-5

Subject Day Date / /

2. Necrobiosis lipoidica.

Sex: Females are affected more

Age 20-40 years.

C/P: One or several sharply, but irregularly demarcated patches usually on the shins. They appear yellowish in the center and violaceous at the periphery

* Histopathology: 2 types of reaction.

(1) Necrobiotic type

(2) Granulomatous type

Q2-6

Subject: _____ Day: _____ Date: / /

x Treatment: ① Controlled D.M

② Intra lesional steroid injection

③ Excision of ulcerated lesions.

④ Aspirin

(3x) Rheumatoid Nodules.

subcutaneous RN occur commonly with rheumatoid arthritis.

Histopathology: several sharply demarcated Foci of fibrinoid degeneration, surrounded by histiocytes in palisade arrangement.

- Lichen amyloidosis
- Prurigo nodularis

B) Non-itchy

- Erythema nodosum
- NBLD
- Ecthyma
- Pretibial myxedema

Treatment

Necrobiosis Lipoidica "NBL" [2]

Sex: Females are affected more (3:1). **Age:** Nondiabetic type: 20-40 years while NBL diabeticorum (NBLD) has a peak incidence between 50-60 years of age.

Clinical features (Figs 9-11)

- One or several ***sharply, but irregularly*** demarcated patches usually on the shins. They appear yellowish in the center and violaceous at the periphery. The center becomes atrophic with telangiectases and may ulcerate. Decreased sensation to pinprick & fine touch, hypohidrosis & partial alopecia can be found within NBL plaques. Hyperkeratotic plugs, at the periphery of lesions, may be seen which represent elimination of necrobiotic material through hair follicles. NBL tends to be slowly progressive but can heal completely with scarring.
- Affection of other part of the body, other than the pretibial area, may occur especially the thighs, hands and face (where the lesions resemble GA) or in the scalp leading to atrophic patches. The latter may occur rarely alone.

Histopathology (Figs 12, 13): 2 types of reactions may occur in dermis:

- ***Necrobiotic type:*** Large areas of necrobiosis of collagen mainly in lower dermis with histiocytes often encircling necrobiotic collagen in dermis in layered fashion (tier-like, parallel to epidermis) often with perivascular plasma cells. Blood vessels show intimal thickening → occlusion in some areas. The infiltrate may show palisade appearance. Scarlet red staining (for lipids) → numerous extracellular lipid granules in areas of necrobiosis of collagen.

Horizontal palisading sandwiches and plasma cells on histology (unlike GA).

- ***Granulomatous type:*** Scattered granulomas composed of histiocytes, epithelioid cells (plasma cells) & giant cells. There is fibrosis but only slight focal necrobiosis of the collagen.


Fig. 12.


Fig. 13.

Figs 12 & 13. Histopathology of necrobiosis lipoidica

Differential diagnosis: NBL differs from GA by:

Presence of a larger number of giant cells.	More pronounced vascular changes.
More extensive collagen degeneration.	More extensive lipid deposition.
Absence of mucin.	Presence of plasma cells in the infiltrate.
Decreased S100 staining within the cutaneous nerves.	

Etiology

- About 65% of patients with NBL have clinical diabetes mellitus → vascular changes (microangiopathy) → necrobiosis of collagen. About 20% of patients with non-diabetic NBL show abnormal cortisone glucose tolerance test and subsequently develop diabetes. However, NBLD is not common in diabetics, occurring only in 0.3% of patients with diabetes.
- Blood vessels deposits of IgM and C3 were found in 50% of patients suggesting an immune complex vasculitis.

Treatment

- Control of DM.
- High potency topical corticosteroid (1st line) or intralesional steroid injection.
- Aspirin + dipyridamole (to ↓ platelet aggregation).
- Excision and grafting of ulcerated lesions.

Rheumatoid Nodules "RN"

Subcutaneous RN occur commonly with rheumatoid arthritis (20% of patients), rheumatic fever and rarely in SLE. They develop near bony prominences of the elbows, hands, ankles and feet. They may undergo central necrosis and ulceration (perforated RN). Rheumatoid factor is almost always found in high titer.

Histopathology: Several sharply demarcated foci of fibrinoid collagen degeneration, surrounded by histiocytes in palisade arrangement in the subcutis.

Pseudo-rheumatoid nodule applied to SC nodule that resemble RN histologically but without arthritis.

Differential histopathological features of the palisading granulomas

	GA	NBL	RN
Necrobiosis	Discrete foci.	Widely scattered & ill-defined.	Deep, massive and sharply defined.
Collagen degeneration	Incomplete.	Hyalinized appearance with areas of fibrosis.	Complete, resembling caseation.
Histiocytes	Well-marked palisading around areas of necrobiosis.	Diffusely scattered without significant palisading.	Sharply defined palisading.
		Intermingled with necrosis	Marked
Fibrosis	No	Several, with tuberculoid or sarcoidal changes.	May be present, very unusual tuberculoid or sarcoidal changes.
Giant cells "granulomatous pattern"	Present but with unusual tuberculoid & sarcoidal changes.	Capillary wall thickening & occlusive vascular changes.	Perivascular lymphocytic infiltrate. Rarely vasculitis.
Vascular changes	Perivascular lymphocytic infiltrate.	Predominantly dermal.	More in subcutis.
Site	Almost in dermis.	+++	+
Fat	±	+	±
Mucin	+++	-	+++
Fibrin	+		

[4] Granuloma Annulare

- Self Limited, chronic necrobiotic Dermal papules arranged in Annular Configuration.

Pathogenesis

unknown etiology.

a) Enviromental triggers: Trauma, insect bite.
Sunexposure, viral infection.

b) Genetic predisposition: Association generalized GA & HLA Bw35.

c) Immunity:
- Delayed-type hypersensitivity
- Th_1 inflammatory reaction → matrix degradation
- release lysosomal enzymes ⇒ elastic Fiber degeneration
- Vasculitis

Clinically

① localized granuloma annulare
- Single or multiple.
- Papule arranged in annular plaque.
- Commonly on the dorsa of hands & feet, elbows, knees & on Fingers.

② Generalized GA:
- Hundreds of Small Circinate lesion on trunk

③ Perforating GA:
- Small papules with Central umbilicated plugs or Crusts

④ SubCutaneous nodular GA maybe mistaken: Rheumatoid nodules (children, but no Arthritis history).

⑤ Patch GA:- patches of erythema on extremities & trunk.

Pathology

- Palisading histocytes
- Focal degeneration of Collagen & elastic fibres.
- Mucin Deposition in Center of palisaded granuloma.
- Vascular changes: Fibrin, C_3 & IgM deposition in vessel walls.

Treatment

[1] Reassurance & clinical observation as the Disease is self-limited with spontaneous resolution within 2 year.

[2] Topical corticosteroid :- High potency with or without occlusion
- intralesional Corticosteroid injection,

[3] Topical Calcineurin inhibitor or imiquimod

[4] other modalities:- - Cryotherapy
- Surgical excision
- Co_2 laser
- Radiotherapy.

[5] Generalized → oral vit E, Topical steroid, Topical tacrolimus.

[6] Severe Case:- Systemic agents - isotretinoin 0.5mg/kg/day
- Dapson 100mg/day
- Antimalarials

...ology ... vesicle. The ... skin should

5 1 Granuloma.

histopathology:.

- there is a central zone of collagen & elastin degeneration surrounded By an infiltrate Composed mainly of histocytes in palisading arrangement or histocytes 3 played Between Collagen Bundles (interstitial Type)

Mucin Can Be seen (within collagen degeneration) as faint Bluish Blue in Routine Stain.

- vAscular changes (include fibrin, C3 and IgM) deposition in vessel wall (detected By direct immuno fluorescence) & occlusion of vAscular lumina ± perivAscular lymphocytes, eosinophils.

Subject: Day: Date: / /

Q6-1

(E) Sarcoidosis of the skin

skin lesions occur in about 25% of patients with systemic sarcoidosis usually at the onset of the disease

* the lesions are usually Firm, brownish-red or purplish papules and plaques with a tendency to annular Formation

* Clinical variants:

① specific ① Maculopapular sarcoid

② plaque Form ③ Nodular Form

Subject: Date: / /

Qb-2

(4) Annular Form (5) lupus pern.o

(6) Subcutaneous nodular sarco:dos:s

(7) Scar sarco:dos:s

(8) Ang:o lupo:d

(9) Uncommon spec:f:c les:ons

(10) Mucosal les:ons.

(11) Non spec:f:c

* Erythema nodosum

* Erythema mult:form

07 Granuloma

Clinical TYPES of Cutaneous Sarcoidosis

Cutaneous Sarcoidosis

Skin lesions occur in about 25% of Pts with systemic Sarcoidosis usually at the onset of the disease.

However, Cutaneous Sarcoidosis can occur without systemic disease

Clinical Varieties:

1) Specific

Maculopapular Sarcoid (miliary sarcoid)

Numerous affecting mainly face & extensor surface of limbs. It is the most Common Cut. lesion (DD: Syringoma). Acute organ involvement such as Sudden hypopigmentation, arthritis, have been associated with this type of eruption.

Plaque form: slightly elevated with flat surface, associated & chronic disease.

nodular form: affecting Proximal Parts of limbs, Trunk & face

Annular form: formed by central healing. They occur mainly on face, scalp, cicatricial alopecia & trunk

Q7 Granuloma

- Lupus Pernio: violaceous smooth & shiny
Plaques on the acral portions of the body
e.g. nose, ear, fingers, forehead.
- nasal involvement with ulceration may occur

- Subcutaneous nodular Sarcoidosis (Darier-Roussy Sarcoid)
- Site: trunk & extremities
- C/P: Deeply seated nodules usually attached to the overlying skin

The skin may be slightly violaceous
- only biopsy can distinguish these from L. Profundus

- S. Car Sarcoidosis: Sarcoidal lesions (resembling keloids) may develop on S. Car sites e.g. of burns, following erythema nodosum or at site of tuberculin or B.C.G. vaccine.

- Angiolupoid:
soft, hemispherical, reddish brown with blue hue
- site: Side of the nose, corner of the eye, inner area of eye brow or on the cheek

- Uncommon Specific lesions: lichenoid, erythrodermic, ichthyosiform, ulcerating, Polymorphous
Photodistributed PS, papulosquamous & verrucous form.

2

Q 7 Granuloma

- Mucosal lesions: Papules or Flat Plaques with hyperpigmented halo. Ulceration may occur, Mouth (hard Palate), vulva or the Conjunctiva may be affected

- Non Specific:

- erythema nodosum:
- Sarcoidosis may 1st appear with erythema nodosum, fever, hilar lymphadenopathy, Migration Polyarthritis & iritis (lofgren's Syndrome).
- The disease subsides within few months without sequelae

- other non specific lesions: Calcification, Prurigo & E.M. ~~hyperkeratosis, onychol~~

- nail changes: (Specific & non specific)
Clubbing, subungual hyperkeratosis, onycholysis & dystrophy ē & ē out underlying bone cysts

~~Specific~~

3

Q 8 Granuloma

- How to investigate a case of Sarcoidosis

lab. findings

- Increase ESR, leukopenia, eosinophilia & Thromb. -ocytopenia
- Hypercalceamia
- Hypergammaglobulinemia, elevated serum alkaline Phosphatase (with liver & bone affection)
- Elevated serum ACE in 60% (diagnostic) but also present in DM & alcoholic liver. it is produced by the epithelioid cells of the granuloma & can be a useful monitor of disease activity.
- X-ray - hilar adenopathy & "Punched-out" lesions of distal Phalanges.
- Fiberoptic bronchoscopy with transbronchial lung biopsy in systemic Sarcoidosis. Bronchoalveolar lavage may be performed for leukocyte differential counts. CD4/CD8 ratio > 3-5 is suggestive of Sarcoidosis

Markers of disease activity

ACE, lysosomes, B2-microglobulin, neopterin, collagenase & fibronectin. Serum level of soluble IL-2 receptors & of TNF-receptor II levels. The serum level of ICAM-1 mirrors disease activity.

8 Q : How to Investigate a Case of Sarcoidosis ?

① CBC : ↑ ESR – esinophilia – Leukopenia – Thrombocytopenia.
② Hypergammaglobulinemia.
③ Hypercalcemia.
④ ↑ ACE → diagnostic produced by epithelial Cell of granuloma – usful monitor of ds. activity.
⑤ – X Ray → hilar adenopathy – punched out lesion of distal phalanges.
⑥ – Fibro-optic bronchoscopy & transBronchial Lung biobsy in systemic Sarcoidosis.

markers of ds. activity :-
ACE – lysozyme – B_2 microglobulin – neopterin – Collagenase – & fibronectin.

9-1 granuloma.

- non-caseating epithelioid cells Tubercles. scattered throughout the dermis with slight admixture of Lymphoid cells at the margin (naked tubercles).

- there is little central fibrinoid necrosis and v few giant cells. Occasionally, the giant cell Contain eosinophilic stellate inclusion Bodies (asteroid Bodies) or round basophilic Laminated inclusions (Schauman bodies) (non specific as may Be present also in TB, leprosy and Berylliosis).

- the epidermis is either normal or atrophic

- Reticulum Stain (Foot's stain):-
  Anetwork of Reticulum fibres surrounding and permeating epitheliod cell granulomas.

Histo Chemical Study:-
shows the presence of lysosomal ~~study~~ enzymes in most of lymphoid cells

thus appear as monocytes and not lymphoid cells.

It was found that the centre of the granuloma is made up of Activated macrophages and OKT4 helper cells.

the periphery of the granuloma has small population of OKT8 suppressor cells.

- DD: Similar histopathological features are present in:
  - TB
  - Tuberculoid leprosy
  - deep fungal Infection
  - Cutaneous leishmaniasis
  - Beryllliosis

- the Kveim test: intradermal injection of 0.2 mL of aheat-sterilized suspension of Sarcoidal Tissue (from spleen or LN)

9-3 Granuloma

histo pathological examination of Test site 6w after injection shows a well defined epithelioid cells Tubercles are found in Case of positive Reaction.

the Test is -ve in 80% of patients of Sarcoidosis, with false +ve reactions in less than 2%. (in Brucellosis, Tuberculosis and Crohn's disease)

- Cortilosteroid may inhibit the Reaction.

9-4 Granuloma.

	Lupus Vulgaris	Tuberculoid leprosy	Sarcoidosis
site →	upper dermis	Lower dermis	upper & Lower dermis
shape →	Rounder or oval	Elliptically elongated "follow nerves"	Rounded
Adenxa →	−	involved	−
Caseation →	±	−	−
lymphocyte →	+	+	−
epidermis →	ulceration	−	-/aTrophy
fibrosis →	+	−	+
special stain →	ZN	Fite	ReTiculin

Page :

Date : / /

Q10 Compare Cheilitis granulomatosa versus Cheilitis glandularis

	Cheilitis granulomatosa	Cheilitis glandularis
C/p	- Recurrent facial swelling especially of one lip & or other lip, forehead, chin or eyelids - Recurrent facial paresis - Lingua plicata "fissured tongue"	- persistent swelling of the lower lip and occasionally upper lip - Squezing of lips → droplets of mucoid fluid.
Histopathology	in the skin. - Diffuse or focal accumulations of either a tuberculoid or lymphoid plasma cellular infiltrate so - small naked epithelioid cell granuloma	in the tongue, salivary glands & Dilated ducts
Squamous cell CA	-ve	Squam cell CA develops in the vermilion border

Page : Date : / /

Q. No 11

Melkersson-Rosenthal S.

- It is also called Cheilitis granulomatosa.

* Characters :-

It is ccc by triad of :

① Recurrent facial swelling (84%) esp. of one lip &/or other lip, forehead or eyelids.

② Recurrent facial pareses (23%), simulating Bell's palsy.

③ Lingua plicata "fissured tongue" in 60% of pts.

- Histopathology :-

Diffuse or focal accumulations of either tuberculoid or lymphoid plasma cellular infiltrate & there are also small "naked" epithelioid cell granulomas as in sarcoidosis.

- Etiology or (Histogenesis) :-

- A relationship to sarcoidosis does not exist
- The granulomas may represent a foreign

2/9

Page : Date : / /

body reaction arising in response to degenerative changes in the tissues, especially the subcutaneous fat.

Treatment :-

- IL steroid
- Dapsone
- Surgical reduction (cheiloplasty) have been used.